Isolation and in vitro characterization of Basal and submucosal gland duct stem/progenitor cells from human proximal airways.

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Authors: Ahmed E Hegab, Vi Luan Ha, Daphne O Darmawan, Jennifer L Gilbert, Aik T Ooi, Yasser S Attiga, Bharti Bisht, Derek W Nickerson, Brigitte N Gomperts

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Public Summary:
Here we describe a method to reproducibly isolate stem cells from the human large airways and a culture system to allow them to become mature, functional airway cells. We also show that the reparative capacity of the human airway stem cells differs based on the histology of the airways and that a subpopulation of the highly reparative airway stem cells expresses a high level of the enzyme, aldehyde dehydrogenase.

Scientific Abstract:
Basal cells and submucosal gland (SMG) duct cells have been isolated and shown to be stem/progenitor cell populations for the murine airway epithelium. However, methods for the isolation of basal and SMG duct cells from human airways have not been defined. We used an optimized two-step enzyme digestion protocol to strip the surface epithelium from tracheal specimens separate from SMG cells, and we then sorted the basal and duct stem/progenitors using fluorescence-activated cell sorting. We used nerve growth factor receptor, as well as a combination of CD166 and CD44, to sort basal cells and also used CD166 to isolate SMG duct cells. Sorted stem/progenitor cells were cultured to characterize their self-renewal and differentiation ability. Both basal and SMG duct cells grew into spheres. Immunostaining of the spheres showed mostly dense spheres with little to no central lumen. The spheres expressed cytokeratins 5 and 14, with some mucus- and serous-secreting cells. The sphere-forming efficiency and the rate of growth of the spheres varied widely between patient samples and correlated with the degree of hyperplasia of the epithelium. We found that only aldehyde dehydrogenase (ALDH)(hi) basal and duct cells were capable of sphere formation. Global inhibition of ALDH, as well as specific inhibition of the ALDH2 isoform, inhibited self-renewal of both basal and duct cells, thereby producing fewer and smaller spheres. In conclusion, we have developed methods to isolate basal and SMG duct cells from the surface epithelium and SMGs of human tracheas and have developed an in vitro model to characterize their self-renewal and differentiation.

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